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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s):	Matthew J. During
Application No:	09/825,713
Filing Date:	April 4, 2001
Entitled:	APPLICATION OF MYELOID-ORIGIN CELLS TO THE NERVOUS SYSTEM
Atty. Docket No:	104036-14

Group Art Unit: 1636
Examiner: K. Katcheves

#16

Certificate of Mailing (37 C.F.R. 1.8(a))

I hereby certify that this correspondence is being deposited with the United States Postal Service Post Office as first class mail in an envelope addressed to: BOX AMENDMENT, Assistant Commissioner for Patents, Washington, D.C. 20231 on the date set forth below.

5 March 2003		By:
Date of Signature and Mail Deposit		Thomas J. Engellenner Reg. No: 28,711

DECLARATION OF DR. MATTHEW J. DURING

PURSUANT TO 37 CFR §1.132

Assistant Commissioner for Patents
Washington, D.C. 20231

Considered
6/30/03
KK

Dear Sir:

I, Matthew J. During, residing at 1512 Spruce Street Apt. 2901, Philadelphia, PA 19102 hereby declare as follows:

1. I am an inventor of the inventions claimed in the above-identified U.S. Patent Application. I am familiar with the claims and the art references that have been cited during the examination of this application.

2. I am presently a Professor of Molecular Medicine and Pathology at University of Auckland in New Zealand. From 1998 through 2002, I served as the Director of the Central Nervous System Gene Therapy Center and Professor at Thomas Jefferson University, Department of Neurosurgery, in Philadelphia, Pennsylvania. From 1989 through 1998, I served on the faculty at the Yale School of Medicine. As the Director of the Gene Therapy & Neurogenetics Laboratory at Yale University from 1993 through 1996, I played a fundamental role in the development of Yale's first gene therapy protocol.

3. I received an M.D. from the University of Auckland School of Medicine in 1982 and underwent training at the University of Auckland (1982-1986) and subsequently at Massachusetts General Hospital (1986-1989). I also served as an attending physician at Yale School of Medicine for several years while I was the Director of the Gene Therapy & Neurogenetics Laboratory there.

4. My experience in this field also includes post-doctoral research at Massachusetts Institute of Technology, Harvard Medical School, and Yale University. For over fifteen years, I have conducted research in the fields of gene transfer and therapy, neuroscience, and molecular biology. I established my own laboratory at the Yale School of Medicine and at Thomas Jefferson University. I presently continue my research at the University of Auckland. As a result of my research, I have authored more than one hundred papers, many of which have been published in peer-reviewed journals such as *Nature* and *Science*.

5. I have read the Office Action mailed November 6, 2002 with respect to the above-identified patent application. I understand that this Office Action rejects the pending claims pursuant to 35 USC §112, first paragraph, for not enabling one skilled in the art to make and use the invention for the entire scope of the claimed invention.

6. I understand that the Examiner has asserted that the invention is enabled for rats and mice, but not for other mammals. I have reviewed the application and believe that the description and figures provide an enabling disclosure of the invention that can be generally used in mammals by someone skilled in the art.

7. Well-characterized animal models are routinely used as the direct precursor to clinical trials and have proven to be highly predictive of human results. In particular, the correlation between rat and/or mouse models of CNS diseases and other mammals has been extensively studied and is frequently relied upon to predict results in humans. For example, studies done in rat and mouse models of CNS diseases have accurately predicted primate and human data in fetal transplant studies.

8. Our patent application uses well-established behavioral models of nervous system disorders, such as Parkinson's disease, to demonstrate the invention. The results disclosed in the application demonstrate that human stem cells of myeloid origin

are capable of migrating from the injection site to the damaged site where they can engraft into the tissue and differentiate into neuronal and glial cells. The application discloses methods for identifying, isolating, culturing, and transplanting human myeloid stem cells into a subject, such that the cells migrate to the damaged site and differentiate into neuronal and glial cells. The studies, which were performed in well-recognized animal models, can be performed, by one skilled in the art, in other mammals to produce similar effects.

9. The findings from the animal-model studies disclosed in our application have also recently been verified in humans. The attached journal article by Mezey *et al.* (*Proc. Natl. Acad. Sci. USA* 100(3): 1364-1369 (2003)) demonstrate that human bone marrow cells, which include myeloid stem cells, can migrate into the brain of a human recipient and generate neurons. The newly generated neurons and microglia were determined to have resulted from the implanted cells. This human data verifies the underlying principle, disclosed in the application, that implanted myeloid stem cells are capable of migrating from the injection site and differentiating into neuronal and glial cells.

10. In summary, the accuracy with which animal models have predicted human results in similar studies, the recent human verification of the principles disclosed in the application, in combination with the application's description of methods for identifying, isolating, culturing, and transplanting human myeloid stem cells into a subject, would enable one skilled in the art to utilize the methods of the invention in other mammals.

11. I further declare that all statements made herein of my knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under § 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Dated: 2/21/03

Matthew J. During, M.D.
Professor
University of Auckland